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Characteristics and Treatments of Patients with Peripheral Arterial Disease Referred to UK Vascular Clinics: Results of a Prospective Registry

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Background. *Peripheral arterial disease (PAD) is often associated with risk factors including cigarette smoking, hypertension and hypercholesterolaemia, and patients have a high risk of future vascular events. Good medical management results in improved outcomes and quality of life, but previous studies have documented sub-optimal treatment of risk factors. We assessed the management of cardiovascular risk factors in patients with PAD referred to specialist vascular clinics.*
Methods. *This was a prospective, protocol driven registry carried out in UK vascular clinics. Patients who were first-time referrals for evaluation of PAD were eligible if they had claudication plus ankle-brachial pressure index (ABPI) $\leq$0.9. Statistical associations between key demographic and treatment variables were explored using a chi-squared test.*
Results. *We enrolled 473 patients from 23 sites. Mean age was 68 years (SD 10) and 66% were male. Mean estimated claudication distance was 100 m, and ABPI was 0.74. Mean systolic blood pressure (SBP) was 155 mmHg, and 42% had a SBP >160 mmHg. Forty percent were current smokers and half had tried to give up in the prior 6 months, but there was no evidence of a systematic method of smoking cessation. Mean total cholesterol was 5.4 (SD1.2) mmol/l and 30% had levels >6 mmol/l. Antiplatelet therapy had been given to 70% and statins to 44%. Prior CHD was present in 29% and these patients had significantly higher use of antiplatelet therapy, statins and ACE-inhibitors.*
Conclusions. *In spite of attempts to raise awareness about PAD as an important marker of cardiovascular risk, patients are still poorly treated prior to referral to a vascular clinic. In particular, the use of evidence-based treatments is sub-optimal, while hypertension and cigarette smoking are poorly managed. More work needs to be done to educate health professionals about the detection and optimal medical management of PAD.*

Keywords: Claudication; Peripheral arterial disease; Risk factors; Smoking; Antiplatelet agents; General practice.

Introduction

Peripheral arterial disease (PAD) is a common and important manifestation of atherosclerosis. PAD affects about 5% of western populations aged between 55 and 74 years and usually presents with intermittent claudication (IC).[1,2] IC can usually be managed conservatively with only 5–10% of patients requiring intervention (reconstructive surgery, balloon angioplasty or amputation) within 5 years of presentation. Patients with PAD are at increased risk of coronary and cerebrovascular events, and more than half of patients with PAD have significant co-existing coronary disease.[3] The risk of cardiac death in patents with IC is 3–4 times greater than those without IC, and accounts for as many as 75% of all deaths in patients with IC.[4,5] Classical risk factors such as smoking, hypertension, hypercholesterolaemia and diabetes are common in patients with PAD and require the same aggressive treatment as patients with coronary or cerebrovascular disease.[2,6]

Previous studies have shown that PAD is poorly managed in terms of providing evidence based

On behalf of the PREPARED (Prospective Registry and Evaluation of Peripheral Arterial Risks, Events and Distribution) Investigators.
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treatments that reduce cardiovascular risk including anti-platelet agents, statins, anti-hypertensives and smoking cessation.[7–10] The reasons for this under-treatment are not completely clear, but appear to be related to a poor understanding of the increased cardiovascular risk associated with PAD, leading to an underestimation of the serious nature of the disease.[11] Over the past few years there has been a concerted effort by professional organisations to raise awareness of PAD, its associated risks and the need for proper management. It is uncertain if these efforts have led to adequate improvements in PAD management in primary and secondary care.[12] We undertook the Prospective Registry of Peripheral Arterial Risks, Events and Distribution (PREPARED-UK) of patients referred from primary care to specialist vascular clinics to understand how they had been treated prior to referral. Since all patients had IC as part of the entry criteria for the registry our assumption was that the treatments on referral provided information on the management of symptomatic PAD in primary care. We report on the baseline characteristics and treatments of these patients. This information may provide a benchmark by which future practice may be improved.

Methods

PREPARED-UK is a prospective cohort study designed to assess characteristics, treatments and outcomes of patients with IC presenting for the first time to Vascular Units in the UK. Follow-up of patients for 2 years is ongoing and will be reported separately, as will information on Quality of Life and health economics. The UK Multi-Centre Research Ethics committee approved the study protocol, patient information sheet and consent form, and these documents were then approved by Local Research Ethics Committees in the participating institutions. Patients were required to give written informed consent before their participation. Patients were also registered, with their consent, with the Office of National Statistics (ONS) for long-term follow-up.

Study design

A list of members of the Vascular Surgical Society of Great Britain and Ireland was obtained and names were sorted by NHS region. We wished to include 25 sites in the study each enrolling 20 consecutive patients. For each region we selected at random a name from the regional centre and 3 additional vascular units in that region. If centres or particular investigators were unable to take part we continued to invite other centres until we had enough centres to take part. Potentially eligible patients with IC were identified through vascular out-patient clinics of the participating hospitals. Participating centres were recognized to have vascular expertise and had access to treadmill testing, duplex scanning, diagnostic and interventional radiology, CT scans, and magnetic resonance imaging (MRI). Two of the centres were running nurse-led claudication clinics. One district hospital had no vascular laboratory while MRI was not available in another.

Eligibility

Patients were eligible if they had a good clinical history of IC occurring within a walking distance of about 400 metres or quarter of a mile, had an ankle/brachial blood pressure index ≤ 0.9, were presenting as a new referral to a vascular clinic of a participating hospital and were able to provide written informed consent. Patients were excluded if they presented with critical limb ischaemia including rest pain, necrosis or ulceration, spinal canal claudication or venous claudication, or if the claudication was incidental to presentation with another major medical condition. Claudication distance was based on patients estimates not on treadmill testing. A current smoker was defined as smoking within the previous 3 months, and an ex-smoker as a history of smoking but not within 3 months of enrolment. No assessments of cotinine levels or carbon monoxide were carried out as part of this study. Clinical assessments and blood test results for biochemistry, haematology and lipid profile were performed as part of routine procedures and not as a specific part of the registry protocol. They were performed in the local laboratories of the collaborating hospitals. Hence these results are not available for all patients.

Study management

A Steering Committee designed and agreed the protocol and the case record forms. The study was coordinated by the Clinical Trials and Evaluation Unit of the Royal Brompton Hospital, London, and the Northern Vascular Unit, Freeman Hospital and University of Newcastle, Newcastle. Centres were trained on study procedures by telephone call and were instructed to identify consecutive eligible patients presenting to the outpatient clinic. Case report forms were completed and any queries or missing data points were resolved by direct contact with the centre.

Statistical methods

This report is of baseline data of the study, and the main aim was to explore associations between demographics and treatments. The study planned to follow patients up for a minimum of two years. We estimated that the rate of death, stroke, myocardial and major limb amputation would be about 5% per annum or 10% over 2 years. A pragmatic sample size assumption would allow comparisons between major subgroups to (e.g. men and women, or prior CHD and no prior CHD). With a sample size of 500 we could detect absolute differences in clinical outcomes of 10% between major subgroups with an alpha error of 5% and beta error of 20% (80% power). We estimated that this sample size would also provide sufficient power to explore associations of age, gender and other important baseline demographic variables on the symptoms and signs of IC, and whether treatment was influenced by these variables. Variables were described as means and standard deviations, or proportions, as appropriate. The main pre-specified subgroup comparison was between patients with and without a history of coronary heart disease (CHD) defined as one or more of the following: prior myocardial infarction (MI), angina, coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI). These groups were compared by the Student's t-test or the chi squared test as appropriate. Other baseline variables of interest were: age, gender, ankle-brachial pressure index (ABPI), systolic blood pressure (SBP), diabetes, hypertension, absolute claudication distance, smoking, antiplatelet and lipid lowering medication. Statistical associations were explored using a chi-squared test, splitting continuous variables into two or more categories as required.

Results

Participating centres

Forty-two centres were invited to take part of which 23 agreed to participate. A total of 473 patients were enrolled between June 2002 September 2003. Nineteen centres enrolled 10 or more patients. The maximum number enrolled at a single centre was 51 and the average per centre was 21 patients. Since some centres enrolled fewer than the 20 patients requested, other centres were requested to enrol more patients in order to reach the pre-specified sample size of 500 patients. Although the intention was to enrol consecutive eligible patients, it seems that a number of centres were not able to achieve this.

Patient demographics and risk factors

The main demographic characteristics of enrolled subjects are given in Table 1. Mean age was 68 (SD 10) years and 66% were male. Mean systolic blood pressure was 155 (SD 24) mmHg, and 54% were being treated for hypertension. Systolic blood pressure >140 mmHg was recorded in 76%, and 42% had SBP >160 mmHg. Twenty percent had a history of prior diabetes (with 5% treated with insulin), 29% had a history of prior coronary artery disease and 20% were working at the time of enrolment.

Table 1. Baseline characteristics

Characteristic	Females, N = 159	Males, N = 319	*p*-value	N = 478*
Age at enrolment, mean (SD) (min − max)	69.7 (9.6) (40, 87)	66.7 (9.6) (34, 93)	**0.001**	68 (9.7) (34, 93)
BMI, mean (SD) (min − max)	26.2 (4.6) (17, 42)	26.7 (4.3) (17, 40)	0.22	26.5 (4.4) (17, 42)
Systolic blood pressure, mean (SD) (min − max)	157.4 (25.2) (90, 220)	153.3 (22.7) (75, 234)	0.08	154.7 (23.6) (75, 234)
<100 mmHg [n(%)]	1 (1)	2 (1)	0.71	3 (1)
100−140 mmHg [n(%)]	37 (23)	75 (24)		112 (23)
140−160 mmHg [n(%)]	47 (29)	113 (35)		160 (34)
160−180 mmHg [n(%)]	46 (29)	80 (25)		126 (26)
>180 mmHg [n(%)]	28 (18)	48 (15)		76 (16)
Diastolic blood pressure, mean (SD) (min − max)	80.8 (11.4) (90, 110)	82.5 (12.4) (50, 130)	0.16	81.9 (12.1) (50,130)
History of diabetes, n(%) Non insulin dependent	16 (10)	56 (18)	**0.031**	72 (15)
Insulin dependent, n(%)	9 (6)	15 (5)	0.65	24 (5)
History of Hypertension n(%)	100 (63)	165 (52)	**0.021**	265 (55)
History of Hyperlipidaemia n(%)	67 (42)	139 (44)	0.77	206 (43)
Angina n(%)	28 (18)	59 (19)	0.81	87 (18)
Prior myocardial infarction (MI) n(%)	18 (11)	51 (16)	0.17	69 (14)
Prior coronary artery bypass graft (CABG) n(%)	10 (6)	34 (11)	0.12	44 (9)
Prior percutaneous coronary intervention (PCI) n(%)	6 (4)	11 (3)	0.86	17 (4)
Any prior coronary heart disease (angina, MI, CABG or PCI)	41 (26)	100 (31)	0.21	141 (29)
Prior cerebrovascular accident (CVA) n(%)	10 (6)	25 (8)	0.54	35 (7)
In paid employment n(%)	15 (9)	79 (25)	<**0.001**	94 (20)

*This is the total number of patients with baseline information. The denominator for each variable ranges from 460 to 473.
Significant values are in bold.

Features of claudication

The mean estimated initial claudication distance (walking distance from start at which the symptoms appeared) was 100 m (interquartile range [IQR] 50–200 m) and mean estimated absolute claudication distance (point at which patient could walk no more and had to rest) was 150 m (IQR 75–250 m) (Table 2). Overall mean ABPI was 0.74, with slightly but non significantly lower values in the left leg compared to the right. Fifty three percent reported symptoms of claudication in both legs.

Smoking status

A history of smoking was present in 84% (39% current smokers and 45% ex-smokers), and in those that gave a history of smoking, estimated mean pack years smoked was 40 (Table 2). About 50% of smokers had attempted to stop smoking in the previous six months, and of the methods used, nicotine replacement therapy and ''will power'' (i.e. attempting to give up without external help or using nicotine replacement therapy) were the most common.

Medications

Seventy percent of patients were on antiplatelet therapy at enrolment and most were taking aspirin at a mean dose of 75 mg, which is the standard dosage used in the UK for cardiovascular risk reduction. Clopidogrel was used in 5% of patients (Table 4). The most common reason for not taking an antiplatelet agent was because it had never been prescribed. Forty four percent were taking a statin, 26% an ACE inhibitor, 18% a beta-blocker, and 29% were on a diuretic.

Results of blood tests

Cholesterol measurements were available for 73% of patients. Mean total cholesterol was 5.4 mmol/L (SD 1.2), and 31% had values $\geq$6 mmol/L. Other blood results including other lipid parameters, glucose levels and creatinine are given in Table 5.

Comparison of patients with prior CHD versus no prior CHD

Patients with a prior CHD history were significantly older, had a greater proportion of diabetes and hypertension, but fewer were current smokers, than those without a history of prior CHD (Table 6). Proportions of CHD patients taking antiplatelets, statins, ACE inhibitors and beta blockers were significantly higher. There was better control of blood pressure among CHD patients as measured by a significantly greater proportion with systolic blood pressure <140 mmHg.

Associations between baseline variables

Apart from the pre-specified subgroup of patients with CHD, other exploratory analyses between baseline variables were undertaken. Differences between men and women are highlighted in Tables 1–6. The main differences include (all $p < 0.01$): women are older, have less paid employment, are more likely to be non smokers. Decreasing ABPI showed a significant association with older age ($p = 0.01$), higher systolic blood pressure ($p = 0.03$), and decreased absolute claudication distance ($p = 0.03$). Antiplatelet and lipid lowering therapies were more frequently prescribed in older patients ($p < 0.01$), those with higher systolic blood pressure ($p = 0.01$), diabetes ($p = 0.01$), hypertension ($p < 0.01$) and smokers ($p < 0.01$).

Discussion

Our findings confirm that in spite of attempts to raise awareness about PAD as an important marker of cardiovascular risk, patients are still poorly managed prior to referral to a vascular clinic. About one third do not receive antiplatelet treatment, half do not

Table 2. Features of claudication

Characteristic	Females	Males	*p*-value	N = 478
Initial claudication distance (m) Median (IQR)*	80 (40, 182)	100 (50, 200)	**0.031**	100 (50, 200)
Absolute claudication distance (m) Median (IQR)*	110 (70, 210)	80 (150, 300)	**0.013**	150 (75, 250)
Ankle brachial pressure index: Left, mean (SD)	0.72 (0.19)	0.71 (0.22)	0.93	0.72 (0.21)
Ankle brachial pressure index: Right, mean (SD)	0.74 (0.19)	0.75 (0.22)	0.48	0.75 (0.21)
Bilateral claudication n(%)	92 (58)	165 (52)	0.21	257 (54)
Previous vascular graft n(%)	1 (1)	8 (3)	0.15	9 (2)
Documented internal carotid stenosis (>50%), n(%)	3 (2)	11 (3)	0.34	14 (3)
Known Aortic aneurysm n(%)	4 (3)	9 (3)	0.85	13 (3)

*Distances estimated by patients and investigators, hence ''rounding off'' is likely.
IQR = inter quartile range.

Table 3. Smoking status and methods used to give up

Description	Females	Males	*p*-value	N = 478
Smoking, n(%)				
Current	62 (39)	123 (38)	**<0.001**	185 (39)
Ex-smoker[1]	56 (35)	165 (52)		221 (46)
Non-smoker	41 (26)	16 (5)		57 (12)
Smoker other (e.g. pipe/cigars)	0 (0)	15 (5)		15 (3)
Pack years smoked, Median (IQR)[2]	37 (21, 50)	40 (30, 60)	**0.003**	40 (26, 55)
Attempted to stop in last 6 months, n(%)[3]	39/71 (55)	71/145 (49)	0.41	110/216 (51)
Method used by the 110 patients, n(%)				
Nicotine replacement therapy	25 (64)	22 (31)	**0.003**	47 (43)
Bupropion	3 (8)	2 (3)	0.23	5 (5)
Counselling	3 (8)	7 (10)	0.39	10 (9)
Other:	13 (33)	43 (61)	**0.006**	56 (51)
Will power or no specific method	10 (26)	42 (59)	**0.001**	52 (47)
Hypnosis	3 (8)	1 (1)	0.13	4 (4)

[1] Ex smoker = prior smoking who has given up >3 months prior to enrolment.
[2] Among those who are current or ex-smokers. 379 patients available for analysis.
[3] Among those who are current or ex-smokers. 211 patients available for analysis.

receive lipid-lowering agents and three quarters do not receive ACE-inhibitors or angiotensin-II antagonists in spite of clear evidence supporting the routine use of these agents in patients with PAD.[13–16] There is concomitant poor management of blood pressure and cholesterol. About 40% of the cohort were current smokers and about half of these have tried to give up within the previous 6 months, but there did not appear to be any systematic approach to the provision of smoking cessation therapies. As expected there were high rates of conventional cardiovascular risk factors and about one third had a history of co-existing coronary heart disease. The latter group were much better treated with antiplatelet, cholesterol lowering and anti-hypertensive treatments. We also found significant associations between ABPI and age, systolic blood pressure and absolute claudication distance.

The benefits of optimally managed hypertension are well established and a low ABPI appears to be an important predictor of morbidity and mortality in the elderly with systolic hypertension.[17,18] In our study 76% of patients had a systolic BP > 140 mmHg and 32% had systolic BP > 160 mmHg. This finding is worrying since systolic hypertension has shown to be linked with the risk of both MI and stroke in the elderly and in patients with PAD, and this risk can be reduced by appropriate treatment.[19] Many hypertensive claudicants will require at least two blood-pressure-lowering drugs to achieve and maintain recommended blood pressure targets (≤140/85 mmHg), and compliance is a major problem.[20] Treatment with an ACE inhibitor has been shown to reduce the risk of major cardiovascular events in patients with clinical as well as subclinical PAD.[21] Both the HOPE study and more recently the ASCOT trial have reported on subgroups of patients with PAD and shown that they obtain the same benefit as other groups of patients with cardiovascular disease without an increase in adverse event rates.[13,21,22] There is little evidence that Beta-blockers should be

Table 4. Medications

Description	Females	Males	*p*-value	N = 478* (%)
Antiplatelet therapy	107 (67)	228 (71)	0.35	335 (70)
Types of antiplatelet (n = 335)				
Aspirin	101 (94)	216 (95)	0.64	317 (95)
Clopidogrel	6 (6)	12 (5)	0.72	18 (5)
Dipyridamole	4 (4)	7 (3)	0.69	11 (3)
Mean dose of Aspirin (mg)	85	90	0.37	89
Reason for not taking antiplatelet n = 143	52 (33)	91 (29)		
History of peptic ulcer or gastritis	6 (12)	8 (9)	0.28	14 (10)
Indigestion	6 (12)	3 (3)		9 (6)
Allergy	0 (0)	1 (1)		1 (1)
Never prescribed/ recommended	29 (56)	65 (71)		94 (66)
Non-compliance	2 (4)	2 (2)		4 (3)
Taking Warfarin	0 (0)	0 (0)		0 (0)
Other	9 (17)	12 (13)		21 (15)
Statin	69 (43)	143 (45)	0.77	212 (44)
Lipid lowering agent (other)	2 (1)	4 (1)	0.99	6 (1)
Warfarin	7 (4)	10 (3)	0.48	17 (4)
Digoxin	5 (3)	10 (3)	0.99	15 (3)
ACE Inhibitor	41 (26)	82 (26)	0.98	123 (26)
Beta blocker	36 (23)	49 (15)	0.05	85 (18)
Calcium antagonist	42 (26)	66 (21)	0.16	108 (23)
Angiotensin II antagonist	17 (11)	15 (5)	**0.01**	32 (7)
Nitrate	21 (13)	34 (11)	0.41	55 (12)
Quinine	13 (8)	12 (4)	**0.04**	25 (5)
Diuretic	64 (40)	74 (23)	**<0.001**	138 (29)
Oral hypoglycaemic	12 (8)	46 (14)	**0.03**	58 (12)
Insulin	9 (6)	17 (5)	0.88	26 (5)

*The denominator varies from 469 to 473 due to some variables with missing values.

Table 5. Blood Results

Description	Females	Males	*p*-value	N = 478*
Cholesterol result available n(%)	122 (77)	229 (72)	0.25	351 (73)
Total cholesterol, mean (SD) mmol/L	5.67 (0.11)	5.28 (0.08)	**0.004**	5.4 (1.2)
<4 mmol/L [n(%)]	9 (7)	29 (13)	**0.036**	38 (11)
4–5 mmol/L [n(%)]	23 (19)	68 (30)		91 (26)
5–6 mmol/L [n(%)]	46 (38)	70 (30)		116 (33)
6–7 mmol/L [n(%)]	26 (21)	43 (19)		69 (20)
>7 mmol/L [n(%)]	18 (15)	19 (8)		37 (10)
HDL, median (IQR) n = 180	1.5 (1.3, 1.8)	1.3 (1.1, 1.5)	<**0.001**	1.4 (0.6)
LDL, median (IQR) n = 112	3.1 (2.5, 3.7)	3.2 (2.3, 4)	0.97	3.2 (1.0)
Triglycerides, Median (IQR) n = 266	1.68 (1.27, 2.50)	1.84 (1.25, 2.85)	0.48	1.7 (1.3, 2.7)
Glucose, Median (IQR) mmol/L n = 265	5.1 (4.8, 5.7)	5.5 (4.9, 6.4)	**0.04**	5.3 (4.8, 6.1)
<5 mmol/L [n(%)]	32 (38)	52 (29)	0.28	84 (32)
5–7 mmol/L [n(%)]	41 (48)	89 (50)		130 (49)
7–10 mmol/L [n(%)]	7 (8)	22 (12)		29 (11)
10–14 mmol/L [n(%)]	2 (2)	13 (7)		15 (6)
>14 mmol/L [n(%)]	3 (4)	4 (2)		7 (2)
Creatinine, mean (SD) μmol/L n = 323	90.4 (22.9)	102.9 (28.5)	<**0.001**	98.9 (27.4)
<60 μmol/L [n(%)]	6 (6)	3 (1)	**0.03**	9 (3)
60–100 μmol/L [n(%)]	64 (61)	121 (55)		185 (57)
100–120 μmol/L [n(%)]	26 (25)	60 (27)		86 (26)
120–150 μmol/L [n(%)]	7 (7)	21 (10)		28 (9)
>150 μmol/L [n(%)]	1 (1)	14 (7)		15 (5)
Haemoglobin, mean (SD) n = 304	13.5 (1.5)	14.6 (1.4)	<**0.001**	14.2 (1.5)
MCV, mean (SD) n = 291	91.2 (5.5)	91.9 (6.6)	0.37	91.6 (6.3)
Platelets, mean (SD) n = 304	283.2 (74.9)	255 (85.8)	**0.005**	264.5 (83.3)
White cell count, mean (SD) n = 302	8.3 (2.2)	8.3 (1.9)	0.96	8.3 (1.9)
CRP, Median (IQR) n = 68	5 (5, 7)	5 (5, 6)	0.42	5 (5, 6.5)

*Blood tests were carried out according to local protocols, hence not all 473 patients had results available for analysis.

specifically avoided in PAD for reasons relating to worsening claudication or precipitating severe ischaemia.[6,23]

Smoking is one of the strongest risk factors for the development of PAD, for progression of disease and a poor outcome.[6,24–27] The 5-year mortality rate for patients with IC who continue to smoke is 40% to 50%.[28] Smoking cessation has been shown to not only reduce disease progression but also the mortality in PAD.[29,30] In our study about 40% were current smokers in contrast to the Euroheart survey of CHD patients <70 years in which 21% reported smoking.[31] Half of the smokers in our study reported trying to give up within 6 months of entry, but a surprising finding was that only a half of those who reported trying to give up had been offered nicotine replacement therapy or smoking cessation counselling. Given that smoking is intrinsically linked to PAD in most patients, much of the risk reduction strategy should be directed to smoking cessation. Likewise the PARTNERS programme found only half of patients with PAD who smoked were prescribed interventions for smoking cessation, indicating a missed opportunity for prevention.[29] It has been shown that smokers are more likely to succeed with the help and support from healthcare professionals, and that combining nicotine replacement therapy and brief advice can improve long-term cessation rates.[32,33] The UK National Institute of Clinical Excellence (NICE) has approved nicotine replacement therapy as cost-effective and recommended that it should be offered to all patients making a serious attempt to stop smoking.[34]

In the current study we also found that there was a strong association between prior CHD history and an increased probability that patients were on antiplatelet therapy, lipid lowering agents, ACE inhibitors or β-blockers. About one third of patients with IC have evidence of coronary and/or cerebrovascular disease.[35,36] It appears that patients with PAD and CHD patients are better treated than those with PAD alone suggesting that use of evidence based treatments in cardiology is better than for PAD. This may be due in part to CHD management being heavily influenced by specialist clinics, whereas PAD is largely managed in primary care.

The most common reason for a patient not being on an antiplatelet agent was that it had never been prescribed or recommended. This is despite good evidence that the use of an antiplatelet agent reduces the risk of future cardiovascular events and death by about 25% in PAD.[16,37] There is evidence from the large CAPRIE study, that clopidogrel reduces the risk of death stroke and MI in patients with cardiovascular disease including PAD more effectively than aspirin.[38] A Consensus Report, which reviewed all the available evidence for antiplatelet therapy in PAD, concluded

Table 6. Comparison of patients with prior CHD history (Prior MI, angina, CABG or PTCA) versus those with no prior CHD history

	Prior CHD N = 141	No Prior CHD N = 337	*p*-value
Age Mean (SD)	69 (8.6)	67 (10.1)	**0.012**
N (%) in subgroups by age			
<60 year	20 (14)	88 (26)	**0.011**
60–<70	46 (33)	108 (32)	
70	75 (53)	141 (42)	
Sex (% male)	100 (71)	219 (65)	0.21
APBI mean (SD)	0.73 (0.17)	0.73 (0.17)	0.70
<0.63	37 (27)	89 (27)	0.60
0.63–<0.75	33 (24)	61 (19)	
0.75–<0.85	34 (25)	93 (29)	
0.85	34 (25)	83 (25)	
Blood Pressure:			
Mean SBP (SD)	151 (24.5)	156 (23.1)	**0.044**
Mean DBP (SD)	80.2 (12.1)	82.7 (12.0)	**0.042**
SBP < 140	47 (34)	68 (20)	**0.002**
SBP 140	93 (66)	269 (80)	
Diabetes (%)	39 (38)	57 (17)	**0.007**
Hypertension (%)	107 (76)	158 (47)	<**0.001**
Smoking			
Current	35 (25)	150 (45)	<**0.001**
Ex-smoker	81 (57)	140 (42)	
Non-smoker	22 (16)	35 (10)	
Other	3 (2)	12 (4)	
Mean (SD) total cholesterol level (mmol/l)	5.1 (1.0)	5.6 (1.3)	**0.001**
Antiplatelet (%)	123 (87)	212 (63)	<**0.001**
Lipid lowering (statin or other) (%)	98 (70)	117 (35)	<**0.001**
ACE inhibitor (%)	54 (38)	69 (20)	<**0.001**
Beta blocker (%)	50 (35)	35 (10)	<**0.001**
Angiotensin II antagonist (%)	8 (6)	24 (7)	0.56

1. Patients with one or more of the following features: prior myocardial infarction (MI), angina, coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI).
2. P values for multiple subgroups (e.g. for age, ABPI, SBP and smoking) are for global comparisons.
3. Calculated from the mean of ABPI from right and left leg.

that antiplatelet therapy should be used routinely in PAD with aspirin as first line treatment, and clopidogrel providing a useful alternative if aspirin was not tolerated.[15] The CHARISMA trial of 15,000 patients with elevated vascular risk randomised to aspirin alone or aspirin plus clopidogrel, has not show any convincing evidence for dual antiplatelet therapy in patients with PAD.[39]

Only about half the patients were taking a statin. Evidence for the benefit of statins in patients with CHD has been available for a number of years, but specific evidence for PAD patients has been largely lacking because they were not included in the large randomised trials. However, in the Scandinavian Simvastatin Survival Study, simvastatin significantly reduced the incidence of new claudication in patients with prior MI or angina.[40] In addition simvastatin and atorvastatin have been shown to improve pain free walking in claudicants.[41,42] Clear evidence of the benefit of statins has now been confirmed in patients with PAD, as well as other groups at risk of cardiovascular events, in the large Heart Protection Study of 20,000 patients which was published during the course of enrolment for our study[14], and the meta-analysis of cholesterol lowering trials.[43] The low use of statins is reflected by high cholesterol levels found, with over 50% having a cholesterol greater than 5 mmol/L.

ABPI showed significant associations with older age, blood pressure and claudication distance. The usefulness of ABPI as a marker of generalised atherosclerosis is well documented and a number of cohort studies have reported a graded inverse relationship of decreasing ankle-brachial index to cardiovascular events.[44,45] There are concerns that ABPI is not a routine measurement apart from in vascular clinics, even though the majority of detection and management of PAD is done in the primary care setting. Calls for wider screening to detect PAD in at risk populations (elderly, diabetics and those with other vascular risk factors) have been made and this may require more training and resources directed to health professionals in primary care.[12] As expected the mean age of women was higher than men, more men smoked and more men were in paid employment.

Our study has a number of limitations. We used a pragmatic design in order to minimise extra work in busy vascular clinics. Patients enrolled were not selected at random from referring practices, and in some of the participating centres, they were not consecutive referrals. For these and other reasons generalising our results to wide populations of PAD patients in the UK and other countries may need to be done with caution. We used information from routine blood results and as a consequence there was missing information, and no central checking of laboratory values. Smoking history was obtained from patients without independent checks using cotinine levels, but previous studies have shown that information on smoking history provided by patients is generally reliable.

Our study provides current evidence that the medical management of patients with PAD still needs improvement.[46,47] Evidence in our study from those patients with co-existing CHD confirms that high rates of preventive treatment can be used in this population given the right motivation and knowledge. Improved blood pressure and cholesterol control, a systematic approach to smoking cessation and other lifestyle changes including exercise and appropriate diets, will help to improve the outlook of patients with PAD.[46,47] In the UK it seems unlikely that vascular surgical clinics will have the resources to deliver this care in its entirety, although this might be possible in other European countries. It is recommended that patients with PAD should be followed up in units

that specialize in vascular care and management of cardiovascular risk factors. These messages must be delivered as a matter of urgency to health professionals diagnosing and managing PAD in primary care, those responsible for health care planning policy, and society at large.

Conflicts of Interest

Shaukat Khan, Nicola Delahunty and Rebecca Mister have no conflicts of interest to declare. Gerard Stansby, Andrew Bradbury and Marcus Flather have received honoraria for speaking, travel expenses and hold research grants from sanofi-aventis and other pharmaceutical companies. Gerry Fowkes has received travel expenses, funds for research and fees for consulting form various pharmaceutical companies.

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